REMARKS/ARGUMENTS

Claims 1, 4, 6 and 8 are pending in the application. In the Office Action dated December 10, 2007, the Examiner rejected claims 1, 4, 6 and 8 under 35 U.S.C. 102(b) as being anticipated by Bachmann et al. (US2003091593 A1 and 2003/0099668 A1) and Takauji et al (2002). The pending claims 1, 4 and 6 have been amended to further define Applicants' invention and to reflect the appropriate Sequence ID numbers.

In view of the amended claims and the remarks that follow, reconsideration and a notice of allowance are respectfully requested.

Amendment to the Specification

Applicants have replaced the original specification with a substitute specification providing all sequence ID numbers disclosed in the specification. No new matter has been added.

Applicants have also amended the application to include the enclosed Sequence Listing, on both paper and compact disc. No new matter has been added. Applicants confirm that the Sequence Listing information recorded in computer-readable form is identical to the written Sequence Listing.

Objection to the Specification

The Examiner objected to the specification for failing to comply with the Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures as set forth in 37 CFR 1.821 through 1.825. Applicants have amended the Sequence Listing to include all the sequences disclosed in the specification. The specification has also been amended to include appropriate labeling of disclosed sequences. No new matter has been added. It should be noted that the claimed oligonucleotide formerly identified as SEQ. ID. NO. 7 has become SEQ. ID. NO. 19.

§102(b) Rejection of Claims 1, 4, 6 and 8 by Bachmann et al and Takauji et al.

In rejecting the above-identified claims under 35 U.S.C. 102(b) as being anticipated by Bachmann et al. and Takauji et al, the Examiner alleges that "[t]he immunostimulatory nucleic acid of Bachmann et al. comprises SEQ ID NO: 7 of the instant application" (Page 4, instant Office Action); and Takauji et al. "discloses the administration of the oligonucleotide g10gacga, [which] comprises SEQ ID NO: 7 of the instant application" (page 5, instant Office Action). Applicants respectfully disagree.

Preliminarily, for a reference to anticipate a claimed invention under §102(b), it must adequately meet the terms of the claimed invention interpreted in light of the specification of the application. As set forth in the statute, the single prior art reference must disclose each and every element of the claim under consideration. Moreover, it cannot be rebuilt or reoriented by the utilization of Applicant's teachings in an attempt to create an anticipatory structure.

Of the pending claims, claims 1, 4 and 6 are independent claims.

Claim 1 recites an immunostimulatory oligonucleotide that consists of the following base sequence: GGGGGGGGGGACGATCGTCG (SEQ ID NO: 19).

Claim 4 recites a pharmaceutical formulation comprising as an active ingredient an immunostimulatory oligonucleotide consisting of the base sequence: GGGGGGGGGGACGATCGTCG (SEQ ID NO: 19).

Claim 6 recites a pharmaceutical formulation comprising as an active ingredient an immunostimulatory oligonucleotide consisting of the base sequence GGGGGGGGGGACGATCGTCG (SEQ ID NO: 19), and further comprising an immunomodulating factor.

Thus, all three independent claims 1, 4 and 6 recite either an immunostimulatory oligonucleotide (claim 1) or a pharmaceutical formulation comprising as an active ingredient an immunostimulatory oligonucleotide consisting of the base sequence GGGGGGGGGGACGATCGTCG (SEQ ID NO: 19).

In contrast, the first cited reference, Bachmann et al. (US2003/091593), discloses a formulation comprising the immunostimulatory nucleic acid G10pt, which has the following base sequence: gggggggggggacgatcgtcgggggggggg ([0329], cited reference). Comparison of the referenced oligonucleotide G10pt and the claimed oligonucleotide reveals two main differences:

1. The referenced G10pt contains 11 "g" at the 5' end and 10 "g" at the 3' end, whereas the claimed oligonucleotide contains 10 "G" at the 5' end and only 1 "G" at the 3' end. The presence of the poly G at both ends of the referenced oligonucleotide chemically distinguishes it from the claimed oligonucleotide, structurally as well as functionally. Indeed, the presence and the length of the poly G sequence affect the activity of the oligonucleotide, as clearly stated in the application:

> "In fact, the consecutive addition of G having a high affinity for the cell membrane to the core sequence "GACGATCGTC" induces a high activity."

(Page 8, lines 30-33, instant application);[1]

> "A DNA sequence composed of consecutive guanines is called a poly G sequence or a G-quartet, and enhances the incorporation of CpG DNA into the cell".

(Page 9, lines 16 to 18, instant application).

2. The referenced and the claimed nucleotides are also chemically distinct because the referenced nucleotide is modified in that it contains sulfur in place of oxygen as one of the non-bridging ligands bonded to phosphorus, whereas the claimed nucleotide is non-modified. This difference is explained in paragraph [0329] of the cited reference, "[S]mall letters indicate

[1] All citations are to the substitute specification filed herewith.

deoxynucleotides connected via phosphorothioate bonds, whereas large letters indicate deoxynucleotides connected via phosphodiester bonds. This modification alters the activities of the nucleotides, as clearly stated in the application:

> "...the thiolation of CpG DNA leads to an attenuated activity of activating NK cells"

(Page 2, lines 28-30, of the instant application);

> "The thiolation of DNA enhances resistance to DNAse, but lowers the immunostimulatory activity because interaction with DNA-binding protein is weakened"

(Page 6, line 33 - page 7, line 1, instant application);

> "Unmodified oligonucleotides are not very resistant to nuclease digestion. However, the administration to mice of thiol-modified CpG DNA having an enhanced DNAse resistance causes fatal side effects. The present invention provides an unmodified CpG DNA that has few side effects, and thus a potential for clinical applications, and a potent Th1 immunostimulatory activity."

(Page 11, lines 8-14, instant application).

In view of the above-described differences that chemically distinguish the referenced oligonucleotide, structurally as well as functionally, from the claimed oligonucleotide, Applicants respectfully submit that the cited reference fails to anticipate the rejected claims 1, 4 and 6, as it fails to disclose each and every element of the claims under consideration.

The second cited reference, Bachmann et al (2003/0099668), discloses immunostimulatory nucleic acids G10-PO and G10-PS (Table 1, page 35, cited reference).

G10-PO has the following base sequence:
GGGGGGGGGGGACGATCGTCGGGGGGGGGG

G10-PS has the following base sequence: gggggggggggacgatcgtcgggggggggg

It should be noted that the G10-PS oligonucleotide is identical to the G10pt disclosed by the first cited reference and thus fails to anticipate the claimed nucleotides for the reasons set forth above.

The referenced G10-PS oligonucleotide is distinct from the claimed oligonucleotide in that it contains 11 "G" at the 5' end and 10 "G" at the 3' end, whereas the claimed oligonucleotide contains 10 "G" at the 5' end and only 1 "G" at the 3' end. As set forth above, the presence and the length of the poly G sequence at both ends of the referenced oligonucleotide distinguishes it from the claimed oligonucleotide, structurally as well as functionally.

In view of the above-described differences, that clearly distinguish the referenced oligonucleotides from the claimed oligonucleotide, Applicants respectfully submit that the cited reference fails to anticipate the rejected claims 1, 4, and 6, as it fails to disclose each and every element of the claims under consideration.

The third cited reference, Takauji et al. (2002), discloses the administration of the oligonucleotide g10gacga, which has the following base sequence: GGGGGGGGGGACGATCGTCGGGGGGGGGG.

The referenced g10gacga is distinct from the claimed nucleotide in that it contains 10 "G" at both the 5' end and 3' end, whereas the claimed oligonucleotide contains 10 "G" at the 5' end and only 1 "G" at the 3' end. As explained above, the presence and the length of the poly G sequence at both ends of the referenced oligonucleotide distinguishes it from the claimed oligonucleotide, structurally as well as functionally.

The above-described difference clearly distinguishes the referenced immunostimulatory nucleic acid disclosed by Takauji et al. (2002) from the claimed oligonucleotide, structurally as well as functionally. Thus, Applicants submit that Takauji et al. (2002) fails to anticipate the pending claims 1, 4 and 6, since it fails to disclose each and every element of the claims under consideration.

Accordingly, Applicants submit that all three cited references fail to anticipate the claimed oligonucleotide as recited in independent claims 1, 4 and 6. Claim 8 depends from claim 6 and therefore is allowable for the same reason. Reconsideration and allowance of the pending claims are respectfully solicited.

Applicants respectfully submit that the application is in condition for allowance. Should the Examiner wish to speak with Applicants' attorney, he is invited to contact the undersigned at the telephone number identified below.

Respectfully submitted,

CHRISTIE, PARKER & HALE, LLP

By _____

John D. Carpenter
Reg. No. 34,133
626/795-9900

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